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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,573	09/16/2003	J. Vernon Knight	D6030D/C/CIP	2987

7590 01/31/2007

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/663,573	KNIGHT ET AL.	
	Examiner	Art Unit	
	Aradhana Sasan	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1229/2006 & 09/18/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Claims 1-19 are being presented for examination.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 12/29/2006 and 09/18/2006 was filed. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the information disclosure statement is being considered by the examiner. See attached copy of PTO-1449.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-19 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,090,407 in view of Burke (US 5,736,156) and Priel et al. (US 5,422,344).

Although the conflicting claims are not identical, they are not patentably distinct from each other. Knight et al. in US 6,090,407, claim a method for treating cancer by aerosol delivery of liposomes of anti-cancer drugs via a jet nebulizer. The anti cancer drugs taxol, taxol –A, mitotane, methotrexate, mercaptopurine, lomustine, interferon, 5-fluorouracil and etopside are claimed. The composition of the liposomes includes dilauroylphosphatidylcholine (DLPC) (Col 2,lines 39-42), although it is not specifically claimed. The concentration of the anti-cancer drug in the liposome is no greater than 1.0mg/ml (Claim 4). A liposome with the ratio of 9-nitrocamptothecin to DLPC of about 1:10 to 1:50 wt:wt (Col 2, lines 34-36) is taught, although it is not specifically claimed.

The instant application has claims for a method of treating cancer by aerosol delivery of liposomes of anti-cancer drugs via a jet nebulizer. The anti-cancer drugs claimed are camptothecin (CPT) or a derivative (9-nitrocamptothecin or 10,11-methylenedioxy-camptothecin). The liposomes of the instant application are comprised of dilauroylphosphatidylcholine (DLPC). The concentration of camptothecin in the DLPC liposomes does not exceed 1.0mg/ml (claims 6 and 12). The ratio of CPT (or its derivative) to DLPC in the liposome of the instant application is also about 1:10 to 1:50 wt:wt (Claims 8, 14, and 15).

As to claims 2-5 of the instant application, an inhalation regimen is inherent when delivering drugs by a nebulized liposomal aerosol to the respiratory tract of a patient.

Although the camptothecin (and its derivatives) are not in the group claimed by Knight et al., they are known anti-cancer drugs. Burke in US 5,736,156 teaches the anti-tumor activity of CPT and its derivatives (Col 1, lines 18-26). Burke further uses CPT in liposomes.

Priel et al. in US 5,422,344 teach the use of CPT as drugs with strong anti-tumor activity (Col 2, lines 42-45) and also teach that a CPT composition can be in the form of an aerosol (Col 4, lines 51-58).

Therefore, the claimed subject matter, i.e. a method of treating cancer by using drugs (CPT and its derivatives) and methods of aerosol delivery of liposomes containing CPT would have been apparent to one of ordinary skill in the art when the teachings of Knight et al. are taken in view of Burke, and Priel et al. One would have been motivated to make a modification of the nebulized liposomal aerosol by adding camptothecin because of the anti-cancer advantage, and DLPC would be used in the liposomal formulation because of the advantage of improved drug output.

5. Claims 1-19 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 10/842,977. Although the conflicting claims are not identical, they are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Giovanella et al. in copending application US 10/842,977 claim a method for treating cancer by delivering camptothecin (or its derivatives 20-S-camptothecin, 9-

nitrocamptothecin or 10, 11-methylenedioxy-camptothecin) in dilauroylphosphatidylcholine (DLPC) liposomes to the respiratory tract of a patient, via a jet nebulizer. Specifically, the final concentration of camptothecin (CPT) or its derivative is no greater than 1.0mg/ml (Claim 1). The weight ratio of CPT (or its derivative) to DLPC is about 1:10 to about 1: 50 (Claim 4).

The instant application claims a method of treating cancer by delivering camptothecin (or its derivatives) in a nebulized liposomal aerosol. The liposome is composed of DLPC and the nebulizer delivers the anti-cancer drug to the respiratory tract of a patient. The concentration of CPT in the DLPC liposome does not exceed 1.0mg/ml (Claims 6 and 12). The weight ratio of CPT (or its derivative) to DLPC is about 1:10 to about 1: 50 (Claims 8, 14, and 15).

As mentioned above, an inhalation regimen (Claims 2-5) of the instant application is inherent when delivering drugs by a nebulized liposomal aerosol to the respiratory tract of a patient.

Since the instant application claims a method for treating cancer by using camptothecin (or its derivatives) containing DLPC liposomes in an aerosol, it is obvious over the claims of the copending application 10/842,977 and thus, they are not patentably distinct over each other.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al. (US 5,049,388), in view of Burke (US 5,552,156), and further in view of Waldrep et al. (US 5,958,378).

The claimed invention is drawn to a method of treating lung cancer or a metastatic cancer to the lung by delivering to the respiratory tract a nebulized liposomal aerosol comprising a dilauroylphosphatidylcholine (DLPC) liposome containing camptothecin (CPT or camptothecin derivatives 20-S-camptothecin, 9-nitrocamptothecin or 10,11-methylenedioxy-camptothecin). A nebulized liposomal aerosol comprising the DLPC liposome containing CPT (or its derivatives) and a method of making the liposome is also claimed.

Knight et al. teach a method of treating a patient by introducing into the respiratory tract aqueous aerosol droplets comprising liposomal medication particles (Claims 6-10). It is also disclosed that suitable lipids for liposomal preparation include various phosphatidyl cholines (Col 8, lines 31-38). Methods of nebulizing the particles of liposomes are also disclosed (Claims 11-15). The medication used in the method of treatment is selected from the group consisting of anti-cancer drugs (Claims 4-5). It is also taught that, "in case of lung tumors of primary or secondary origin, the tumor masses would be the site of deposition of aerosol interacted liposome anti-cancer drugs" (Col 17, lines 15-17). The advantage of using the liposomes is that "when the liposome permeability barrier is damaged, such as during aerosolization, the drug is not

prematurely released from the liposome" (Col. 4, lines 7-11). Knight et al. do not teach the use of camptothecin (or its derivatives) in the liposomal composition.

Burke teaches liposomes comprising of camptothecins, including 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin. Burke teaches that any lipid that can form a liposome could be used for the camptothecin containing liposome (Col 6, lines 16-18). Burke does not include the step of delivering the camptothecin containing liposomes by an aerosol. Burke does not teach liposomes made with DLPC.

Waldrep et al. (US 5,958,378) teach delivering anti-cancer compounds, of which camptothecin is a known example. Waldrep et al. teach a liposome aerosol containing a drug and using DLPC in the liposome formulation (claims 5, 11, 14 and 15). Waldrep et al. state, "the aerosol drug output could be improved through the utilization of liposomes formulated with low phase transition temperatures, such as DLPC" (Detailed Description of Invention, Col 4, lines 27-31). The weight ratio of drug to DLPC in Waldrep et al. ranges from 1:7.5 to 1: 15 (claims 4 and 5). The instant application has the weight ratio of camptothecin (or derivative) to DLPC of about 1:10 to about 1:50 (instant claims 8, 14, and 15). Thus, the weight ratio given in the prior art overlaps with that given in the instant claims.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the method of treating cancer by using the nebulized liposomal aerosol containing anti-cancer drugs taught by Knight et al. with the camptothecin containing liposomes of Burke in view of the DLPC liposome aerosol delivery (with improved drug output) of Waldrep et al. One would have been motivated

to add the camptothecin (or its derivatives) to the liposomal-drug composition because of the anti-cancer advantage, and DLPC would be used in the liposomal formulation because of the advantage of improved drug output. As mentioned previously, an inhalation regimen (Claims 2-5) of the instant application is inherent when delivering drugs by a nebulized liposomal aerosol to the respiratory tract of a patient.

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

1. It does not identify the citizenship of inventor Claire Verschraegen.

2. It does not identify the complete mailing address of inventor Claire Verschraegen. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

Conclusion

1. No claims are allowed.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Friday from 7:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang or Cecilia Tsang, can be reached at 571-272-8011 and 571-

272-0562 respectively. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600